to TB treatment, as children have lower drug exposures when given the same mg/kg dose as adults of many TB drugs,[2] and updated World Health Organization (WHO) guidelines now recommend higher doses of the first-line TB drugs in children.[3]

We do not agree that our report provides conclusive support for routine individualized dosing of TB drugs in children. In our case report, many factors other than pharmacokinetic variability contributed to the poor outcome. The child had extensive pulmonary disease and should have received ethambutol, which may have provided additional protection against resistance acquisition. Drugs were under-dosed; using local weight-banded dosing based on new WHO recommendations, this child should have received isoniazid 90 mg (11.4 mg/kg), rifampin 90 mg (11.4 mg/kg), pyrazinamide 250 mg (31.6 mg/kg), compared with the much lower mg/kg doses the child actually received. The 2-month mycobacterial culture and drug-susceptibility result showing isoniazid resistance should have prompted a change in treatment. This child's poor treatment response should have resulted in additional investigations or referral. These failings are at a health system level, and appropriate application of existing tools, without the need for individualized dosing, may have averted this poor outcome. We would be concerned with the feasibility of routine dose individualization given the weak health system described in our case, which hardly seems capable of supporting individualized drug dosing for all children with TB. Finally, the use of crushed or split adult tablets adds another challenge to accurate dosing and may reduce drug palatability. The child in our case was frequently vomiting his medications, further contributing to the inadequacy of his treatment. Child-friendly, palatable TB medications are an urgent priority.

We are not in principle against individualized dosing and care, but given the likely cost and workload associated with routine therapeutic drug monitoring and individualized TB drug dosing, a pragmatic randomized controlled trial evaluating the impact, cost effectiveness, and feasibility of such a strategy in resource-limited high TB burden settings would be very informative. Early assessment of the WHO newly recommended doses of first-line drugs for young children found the resulting concentrations to fall well within the usually suggested range for efficacy.[2] We would argue that in pediatrics the priority is to understand TB drug pharmacokinetics in children of all ages, and designing optimized, pragmatic, feasible dosing strategies to provide the best possible, safe drug exposure in children. Our case also argues for greatly increased efforts at health system strengthening to optimize all aspects of TB care for children.

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Severity of Invasive Pneumococcal Disease in Children Caused by Susceptible and Nonsusceptible Isolates

To the Editors:

In the post-pneumococcal conjugate vaccine era, there has been an increase in non-vaccine serotypes causing invasive pneumococcal disease (IPD), including penicillin nonsusceptible *Streptococcus pneumoniae* (PNSP). The prevalence of PNSP causing IPD is increasing,[1] and antimicrobial resistance of these isolates has been hypothesized to provide a survival advantage.[2] Multidrug-resistant strains have also been associated with a 500% increase in cases of acute mastoiditis, and such cases were more likely to present with subperiosteal abscess and to require intraoperative mastoidectomy.[3] We hypothesized that PNSP may also correlate with increased severity of IPD.

We analyzed data of childhood IPD in Massachusetts that was based on state laboratory surveillance data from 2007 to 2012. Outcomes compared were characteristics of IPD, including patient demographics, clinical features, microbiologic features and comorbidities. A case of IPD was defined by a positive culture for *S. pneumoniae* from a normally sterile site. Penicillin intermediate and resistant isolates, based on current Clinical Laboratory Standards Institute breakpoints, were grouped as PNSP. We compared outcomes of PNSP cases with cases caused by penicillin-susceptible *S. pneumoniae* (PSSP). Patient characteristics were compared using the Fisher's Exact test for categorical variables, and the Wilcoxon or Kruskal–Wallis test for continuous variables. This study was approved by the Institutional Review Boards of the University of Minnesota and the Massachusetts Department of Public Health.

There were 253 cases of IPD from 2007 to 2012 in Massachusetts children ≤5 years of age. Penicillin susceptibility results were available for 239 of 253 isolates (94.5%): 183 were PSSP (76.6%) and 56 were PNSP (23.4%). Of these, 56.4% of patients with IPD caused by PSSP were hospitalized compared with 56.6% of patients with IPD caused by PNSP ($P = 1.000$). Length of hospitalization was a median of 1 day (range 0–42 days) for PSSP IPD cases, compared with a median of 2 days (range 0–14 days) for PNSP IPD cases ($P = 0.931$). There was also no difference in comorbidity ($P = 0.46$), mortality ($P = 0.69$), the number of cases who were readmitted ($P = 0.44$) or who were up-to-date on pneumococcal immunization ($P = 0.35$), between the 2 groups.

Our analysis supports that children with IPD because of PNSP have similar outcomes to cases caused by PSSP. This is similar to findings in other studies where there was no difference in clinical presentation and outcome between patients with PSSP and PNSP isolates.[4] In addition, neither comorbidity nor pneumococcal conjugate vaccine immunization appear to be

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risk factors for invasive disease caused by a PNSP isolate. Although our study is limited by missing data within the cohorts, our study's strength is that it is based on statewide, population-based data that suggest that IPD outcome is not associated with penicillin susceptibility.

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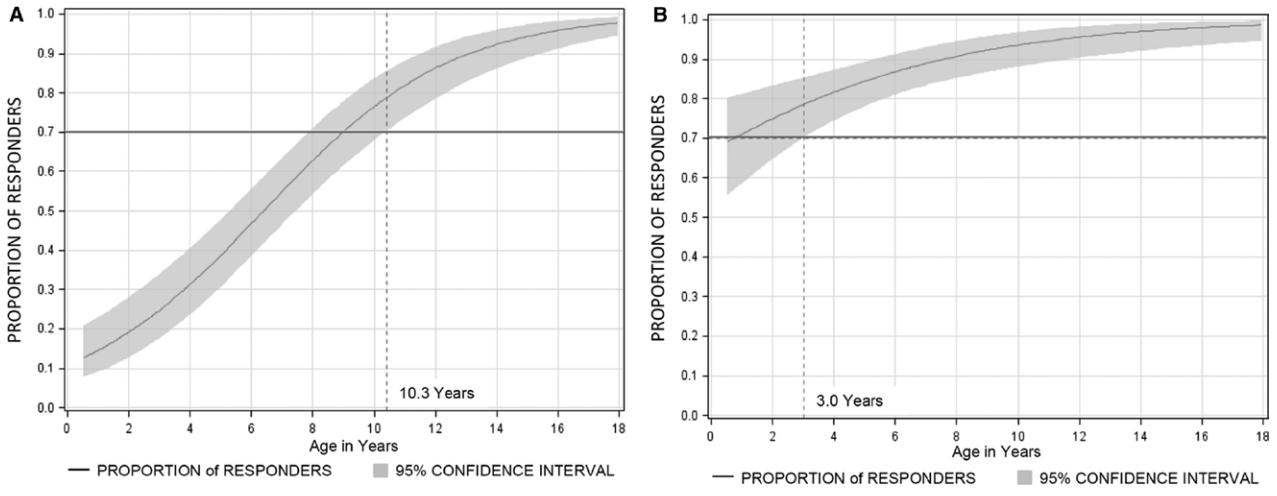
ERRATUM

Clinical and Immune Responses to Inactivated Influenza A(H1N1)pdm09 Vaccine in Children: ERRATUM

In the article on page 865, volume 33, issue 8, a figure is incorrect. The part A and B of Figure 2 were reversed. There was also an error in the horizontal lines of the figure, the dashed line should be solid. The corrected figure is available below.



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Kotloff KL, Halasa NB, Harrison CJ, et al. Clinical and Immune Responses to Inactivated Influenza A(H1N1)pdm09 Vaccine in Children. *Pediatr Infect Dis J*. 2014;33:865–871.